SUMMARY OF SAFETY AND PROBABLE BENEFIT

I. General Information

Device Generic Name: Spinal Fixator

Device Trade Name: Telescopic Plate Spacer (TPS) Spinal System

Applicant's Name and Address: INTERPORE CROSS International
181 Technology Drive
Irvine, CA 92618

Humanitarian Device Exemption (HDE) Number: H990008

Date of Humanitarian Use Device Designation: June 15, 1999

Date of Panel Recommendation: Not applicable (Refer to Section XII for discussion)

Date of Good Manufacturing Practices Inspection: August 1999

Date of Notice to Applicant: MAR 9 2000

II. Indications for Use

The INTERPORE CROSS International Telescopic Plate Spacer (TPS) Spinal System implants are intended to replace vertebral body structures following a vertebrectomy/corpectomy of the spine for metastatic spine disease in the cervical and/or cervico-thoracic spine (C_3-T_2). The TPS Spinal System implants are intended to correct spinal alignment and stabilize the spinal operative site during fusion. TPS Spinal System implants attach to the spine anteriorly by means of their trapezoidal shape and by screws joined with a plate and spacer component.

III. Individualization of Treatment

Patients must meet the following criteria:

1. Skeletally mature.
2. Demonstration of metastatic disease in the cervical and/or cervico-thoracic spine (C_3-T_2)
3. One or two contiguous vertebral bodies require replacement due to metastatic disease
4. Minimum life expectancy ≥ 3 months; and
5. One of the following:
   A. Spinal instability, i.e., ≥ 5° angulation or ≥ 3mm subluxation or compression fracture.
   B. Neurological deficit; compromised reflexes or sensory motor loss, or decreased fecal or urinary continence, where the patient is considered ineligible for or an inappropriate candidate for immediate treatment with (further) chemotherapy, immunotherapy, radiation therapy or steroid therapy alone.
   C. Patient is imminently unstable and at imminent risk of neurological injury by virtue of erosive destruction of the spine, where the patient is considered ineligible for or an appropriate candidate for immediate treatment with (further) chemotherapy, immunotherapy, radiation therapy or steroid therapy alone.
   D. Severe intractable pain, not relieved by medication, pain is > 80 on the 101 NRS Scale, where the patient refuses the morphine pump and is considered ineligible for or an inappropriate candidate for immediate treatment with (further) chemotherapy, immunotherapy, radiation therapy or steroid therapy alone.
   E. Sole recurrence of tumor, where the patient is considered ineligible for or an inappropriate candidate for immediate treatment with (further) chemotherapy, immunotherapy, radiation therapy or steroid therapy alone.

A diagnosis of spinal metastasis may be made based on either MRI signal changes suggestive of spinal or epidural lesions, or myelogram and computerized tomography (CT) showing spinal or epidural lesions.

IV. Device Description

The INTERPORE CROSS International Telescopic Plate Spacer Spinal System implants function as a single construct that combines an anterior plate and an intervertebral column spacer. The TPS Spinal System is composed of seven components: one (1) female chamber, one (1) male chamber, one (1) set screw and four (4) bone screws. The TPS Spinal System implants are made from medical implant grade titanium alloy as described by ASTM Standard F-136 (Ti 6Al-4V ELI) and are available for one- and two-level vertebrectomies/corpectomies. A one-level cervical vertebrectomy/corpectomy device telescopes in length from 22.3 mm to 29.4 mm; a two-level cervical vertebrectomy/corpectomy device telescopes in length from 33.5 mm to 49.8 mm.

V. Contraindications, Warnings and Precautions

CONTRAINDICATIONS

None known.

WARNINGS and PRECAUTIONS can be found in the Professional Labeling (See Attachment 1)

VI. Adverse Effects of the Device on Health

POTENTIAL ADVERSE EFFECTS

The INTERPORE CROSS International TPS Spinal System has not been tested in clinical trials, and there are no data available on actual adverse effects from its use.

The potential adverse effects that may occur with the use of this device may be the same as those that can occur with vertebral body reconstruction surgery for metastatic disease using alternative means. These include, but are not limited to, the following:

Device related effects, such as
- Bending, loosening or fracture of the implants or instruments
- Metal sensitivity to foreign body including possible tumor formation
- Skin or muscle sensitivity
- Nonunion or delayed union
- Bone loss due to resorption or stress shielding
- Bone fracture at, above, or below the level of surgery
- Malalignment of anatomical structures, including loss of proper spinal curvature, correction, reduction and/or height
- Inability to resume activities of normal daily living

Surgery or surgical approach related effects:
- Skin breakdown and/or wound complications
- Bursitis
- Infection
- Hemorrhage of blood vessels and/or hematomas
- Dural tears
- Cerebral spinal fluid leakage
- Nerve or vascular damage due to surgical trauma, including loss of neurological function

- Radiculopathy
- Paralysis
- Urological and/or reproductive system compromise including sterility, impotency and/or loss of consortium
- Pain or discomfort
- Stroke
- Death.

VII. Alternative Practices and Procedures

Present methods for treating instability following a vertebrectomy or corpectomy for metastatic cervical spinal disease include spanning the defect with polymethylmethacrylate (PMMA) bone cement or bone graft with or without anterior and/or posterior instrumentation. Currently, there are no PMMA bone cements on the market that are intended for use in reconstruction of the cervical spine following vertebrectomy or corpectomy for metastatic tumors. Anterior plates are used following vertebral corpectomy for fracture, instability, compression of neural elements (spinal cord, nerve roots), and for severe intractable pain arising from vertebrae which are abnormal by virtue of biomechanical or structural composition or by dysfunctional relationships with adjoining vertebrae. Anterior instrumentation includes plates with screws, and rods with screws. Posterior instrumentation may be accomplished with wires alone or with the addition of bone graft, but this does not provide optimum stabilization.

There are no devices on the market intended to replace the vertebral body in the cervical spine. Reconstruction of a cervical vertebra with bone graft with supplemental instrumentation has limited use in the treatment of metastatic disease because the use of adjuvant radiation therapy or chemotherapy following surgery may compromise the ability to incorporate the autografts or allografts used to span the defect.

VIII. Marketing History

There is no prior marketing history for this device.

IX. Summary of Studies

Non-clinical laboratory studies (mechanical, cadaveric, and animal testing) were conducted using the TPS Spinal System. Clinical studies using the TPS Spinal System implants have not been conducted. The following is a summary of the testing that was conducted using this device.

A. Biocompatibility

The TPS Spinal System implants are manufactured from titanium alloy, a well-known implant grade material per ASTM F-136. History of the safe use of this material in similar clinical applications provides assurance of the biocompatibility of the device.

B. Mechanical Testing

The results of the static and fatigue testing indicate the device should have adequate mechanical properties for use in the cervical spine when the patient is in need of a vertebral body replacement following vertebrectomy/ corpectomy for metastatic spine disease. The safety concerns for this device-type include device component disassembly, screw pull-out, and device breakage due to compression, tension, or torsional loading. Table 1 summarizes the mechanical test results.

The static strength of the device was tested in compression, tension and torsion, and the fatigue strength was tested in compression and torsion. The average ultimate compression bending load was 724 N, an order of

magnitude greater than the average weight of the human head reported in the literature[1,2]. The yield torque strength for the TPS device is 22.7 N-m. This is sufficient to withstand worst-case torque to failure load for the intact cadaveric cervical spine. The run-out load in torsional fatigue testing was 5.1 N-m at 5 million cycles without failure, and the run-out load in compression bending fatigue testing was 89.0 N to 10 million cycles. These tests demonstrate sufficient device integrity and strength for the expected *in vivo* loads for this device for the given indications.

The static bone screw back out force testing demonstrated that the threaded locking mechanism was even stronger than the yield strength of the female component. Thus, screw-female component disassembly is unlikely to occur. The static and fatigue strength of the TPS device in compression bending, tension bending, and torsion was found to be greater than a legally marketed anterior plate device that has similar indications for use. In addition, the static bone screw back out force from the TPS device was significantly greater than that of other legally marketed anterior plate devices intended for use in metastatic tumor patients.

Table 1

Name of Test	Test Standards (if appropriate)	Results
Static Compression Bending Mechanical Test of the Telescopic Anterior Plate/Spacer (TPS) Cervical Device	ASTM F1717	The mean ultimate compression bending load was 724 N ± 18.4 N.
Static Tension Bending Mechanical Test of the Telescopic Anterior Plate/Spacer (TPS) Cervical Device	ASTM F1717	The mean ultimate static tension bending load was 384 N ± 33.3 N.
Static Torsion Mechanical Test of the Telescopic Anterior Plate/Spacer (TPS) Cervical Device	ASTM F1717	The mean yield torque was 22.7 N-m ± 0.95 N-m.
Compression Bending Fatigue Mechanical Test of the Telescopic Anterior Plate/Spacer (TPS) Cervical Device	ASTM F1717	The run-out load was 89.0 N to 10 million cycles.
Torsional Fatigue of the Telescopic Plate Spacer (TPS™) Spinal System Cervical Implant		The run-out load was 5.1 N-m to 5 million cycles without failure.
TPS Spinal System Cervical 2-Level Design Comparison Mechanical Testing vs. Finite Element Analysis		Simulation of failure modes observed during mechanical testing.
Fracture and Removal Torque of the Cervical Telescopic Anterior Plate/Spacer (TPS) Set Screw		Fracture torque of the set screw was 35.7 in-lb. The removal torque was 32.3 in-lb.
Static Bone Screw Back Out Force for the Telescopic Anterior Cervical Corpectomy Plate/Spacer and Synthes Cervical Spine Locking Plate		The mean static screw back out force was 23.7 lbf. for the TPS screw and 13.5 lbf for the Synthes screw .
Static Bone Screw Pull-Out Force for the Cervical Telescopic Anterior Plate/Spacer (TPS) Implant with a Threaded Locking Mechanism, Crimping Tab Blocking Mechanism and No Applied Locking Mechanism		Mean pull-out force of the threaded locking mechanism was 105.0 lbf ± 12.2 lbf. Mean pull-out force of the crimping tab blocking mechanism was 110.4 lbf ± 6.0 lbf.

[1] Beier, G., Schuck, M., Schuller, E., Spann, W.: Determination of Physical Data of the Head. I. Center of Gravity and Moments of Inertia of Human Heads. Scientific Report, No. 1, February 1, 1975-September 30, 1978, Munich University.

[2] Brunnstrom, S.: Clinical Kinesiology, Third Edition. F.A. Davis Company, 1975.

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Static Bone Screw Back Out Force for the Cervical Telescopic Anterior Plate/Spacer (TPS) Threaded Locking Mechanism		Mean static bone screw back out force >500 lb.

C. Cadaver Testing

A cadaver study was conducted using the TPS Spinal System to evaluate restoration of vertebral height and spinal alignment and to estimate the implant pullout force.

Vertebrectomies/corpectomies were performed on three cadavers at C4, C7-T1, and C3-C4, respectively. Fluorochrome pictures were taken to verify implant fit, restoration of vertebral height, and spinal alignment. The result in all three cases was restoration of normal vertebral height and alignment. Stabilization of the defect site was achieved. There was no observed movement of the implant in any of the cases, including the bone screws, when an anterior pullout force was applied.

D. Animal Studies

An animal study[3] was conducted to compare the performance of the Telescopic Plate Spacer (TPS) Spinal System and a legally marketed anterior plate device when used for corpectomies. Range of motion, radiographs, and histology were used for comparison.

A goat model was chosen because of the similarities (mechanical, anatomical, and biochemical) to the human cervical spine. Two groups of six animals were randomly divided and implanted with the TPS Spinal System and the anterior plate device. Discectomies were performed at C3-C4 and C4-C5 levels and a partial corpectomy was performed at C4 in both groups. In the TPS group, bone chips removed from the corpectomy site were packed firmly into the TPS device. The implant was then placed into C4, distracted against the adjacent endplates, and secured using four bone screws. In the anterior plate device, a rib graft was obtained from the goat and inserted between C3 and C5. The anterior plate device was secured using four screws. Fluorochrome markers were given at 24, 25, 26, and 27 weeks post-implantation. The animals were euthanized after a total implantation period of 28 weeks.

Good fusion was indicated by the presence of new bone (both radiographically and histologically), the presence of healthy tissue, near normal bone density and lack of chronic inflammatory cells or extensive encapsulation. The range of motion at adjacent levels for either group did not change. Radiographs of the harvested specimens showed bone within the TPS device and at the posterior aspect of the anterior plate device. Fluorescent and light microscopy confirmed the radiographic findings, and showed new bone growth within the TPS device and new bone growth just dorsal to the legally marketed anterior plate device

X. Conclusions Drawn from Studies

The history of the safe use of this material in other spinal implants having similar clinical indications provides assurance of the biocompatibility of the device. Performance testing to assess mechanical properties demonstrates that the design is appropriate for the proposed intended use. The cadaver study demonstrated that the device could be implanted using the suggested surgical technique. The animal study demonstrated safety of the device in addition to the appropriateness of the design for the intended use.

The preclinical studies (mechanical, animal and cadaver studies), provide reasonable assurance that the device materials and design are safe and appropriate for the proposed intended use. The information provided in the HDE indicates that the Telescopic Plate Spacer (TPS) Spinal System will not expose patients to an unreasonable or significant risk of illness or injury, and that the probable benefit to health from the use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

[3] Mega JE, Moore BS, Marchek CP, et.al. Telescopic Anterior Plate Spacer: *In Vivo* Study Caprine Model. Poster Exhibit at the North American Spine Society Meeting, October 1998.

XI. Risk/Benefit Analysis

Present methods for treating instability following a vertebrectomy or corpectomy for metastatic cervical spinal disease include spanning the defect with polymethylmethacrylate (PMMA) bone cement or bone graft with or without anterior and/or posterior instrumentation. Currently, there are no PMMA bone cements on the market that are intended for use in reconstruction of the cervical spine following vertebrectomy or corpectomy for metastatic tumors. Furthermore, extreme caution must be observed when injecting the PMMA bone cement to prevent contact between the cement and the thecal sac because the polymerization of the cement produces a significant amount of heat that can injure the spinal cord. The use of adjuvant radiation therapy or chemotherapy following reconstructive surgery may compromise the ability to incorporate bone autografts and allografts used to span the defect and thus may limit their use in the treatment of metastatic disease. The Interpore Cross TPS Spinal System allows for the use of autograft and allograft within and around the device, but the stability of the construct does not depend on the biological incorporation of the bone graft. The PMMA and bone graft constructs require supplemental anterior and/or posterior instrumentation to provide adequate stabilization of the spine. Posterior instrumentation requires additional surgical incision and operative time. The Interpore Cross TPS Spinal System incorporates an anterior plate with a vertebral body spacer, allowing the implantation of a single device for spinal stabilization. No additional surgeon training is required because the surgical procedure utilizes the same anterior approach as anterior fusion and discectomy procedures, and the procedure is similar to the present methods of tumor resection and reconstruction with cement or bone with anterior plate and screws.

XII. Panel Recommendation

This HDE was not taken to a meeting of the Orthopedics and Rehabilitation Devices Panel because other marketing applications for lumbar vertebral body replacement devices and anterior cervical plating systems have been cleared for similar indications. It was determined, therefore, that the clinical issues raised by this HDE are similar to those previously reviewed by this Panel.

XIII. CDRH Decision

CDRH determined that, based on the data submitted in the HDE, the Interpore Cross TPS Spinal System will not expose patients with metastatic disease in the cervical and/or cervico-thoracic spine (C_3-T_2) to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risks of illness or injury, and issued an approval order on MAR 9 2000

XIV. Approval Specifications

Directions for use: See the Labeling (Attachment 1).

Indications for Use: See section II above.

Hazards to health from the use of the device: See the Warnings, Precautions, and Adverse Effects Section in the Labeling (Attachment 1).

XV. Publications and Other Outside Information

Mega JE, Moore BS, Marchek CP, et.al. Telescopic Anterior Plate Spacer: *In vivo* Study Caprine Model. Poster Exhibit at the North American Spine Society Meeting, October 1998.